EXHIBIT A

ABBOTT LABORATORIES
RESEARCH DEPARTMENT

BOOK NO. 61,959

PROJECT HCV antigen test

EXP. OR CODE NO.

There have been recent indications that HCV core proteins can be detected in serum of HCV infected individuals, most notably the publications from Tonen Corporation (Tanaka et al, Journal of Hepatology 1995 23: 742-745; and Aoyagi et al, in the Journal of Clinical Microbiology 1999 37:1802-1808. There have been no published disclosures pertaining to an antigen/antibody combo test for detection of exposure to HCV to date. There are several possible methods for devising a combo HCV test, allowing detection of both antibodies and antigens associated with exposure to HCV. Current antigenic targets for the antibody test include recognition of viral proteins derived from several different open reading frames of the virus including core + envelope proteins as well as proteins from nonstructural regions designated as NS (nonstructural) 2, NS3, NS4 and NS5. Commercialized tests currently utilize HCV proteins from NS3, NS4 and/or NS5.

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A potential combo test would continue to utilize one or more virally derived proteins from HCV for antibody detection but would also employ antibodies generated against HCV proteins to develop an antigen sandwich assay which captures HCV proteins on a solid phase (microcellulose, microparticles, polystyrene plate or bead) and then further detects the captured protein with a labeled antibody. One of the most likely targets for detection of HCV antigens is the HCV core protein. While Toren corporation has clearly demonstrated utility of an HCV antigen test, there has been no clear indication of a combo test being developed. For this reason, the following proposal is made - Abbott Labs would develop an antibody/antigen combo test allowing simultaneous detection of antibodies & antigens associated with exposure to HCV. In one example of this combo assay a solid phase would be coated with HCV protein (NS3, NS4 and fragments of the HCV core protein) and also coated with antibodies to HCV. (continued on page 6)

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BOOK NO. 91505

PROJECT HCV antigen test

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This solid phase would capture antibodies to HCV or would also capture HCV proteins (e.g. Core protein). The captured antibodies (that were captured due to antibodies binding to HCV proteins) would be recognized by a second antibody (e.g. goat anti-human IgG) that is labeled with a reporter molecule (horseradish peroxidase, acridinium, biotin etc). allowing detection of antibodies directed agst the solid phase-bound proteins derived from HCV.

The captured antigens would be recognized in one example of the combo assay by specific antibodies (e.g. monoclonal antibodies) against the core protein. this specific antibody would be labeled with a reporter molecule (horseradish peroxidase, BIOTIN, acridinium) to allow detection of the bound antigen.

One of the important differences between the combo test for HCV and HIV as proposed here is that one continues to be able to detect antibodies to core and core antigen at the same time. In order to do this successfully, the core protein needs to be re-engineered. See page 7

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RESEARCH DEPARTMENT

PROJECT HCV antigen test

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The core protein of HCV consists of 191 amino acids. For detection of antibodies to HCV only segments of the core molecule would be needed. For example it is known that there are epitope associated with antibody detection at amino acids 9-88 based on 11 tested serums. Thus, in one version of a combo assay the solid phase would be coated with - NS3, NS4 +/or NS5 proteins and a modified core protein (containing needed epitopes) as well as one or more monoclonal antibodies (or possibly polyclonal antibodies to core). See Figure on page 7. Further the conjugates would recognize the bound antibodies (captured with specific antigen) or bound antigens (captured with specific antibodies). The candidate core proteins would be: recombinant core proteins (aa 1-100, aa 1-120, aa 8-89, aa 9-99 etc) with monoclonal antibodies recognizing epitopes outside of the regions recognized by antibodies in human serum. Alternatively one could use peptides 6 mers or greater covering major epitopes between amino acids 1-100. Further, the antigens on the solid phase could be re-engineered to include amino acid substitutes, deletes, etc.

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Schematic of Potential HCV Combo Antibody/Antigen Test

Liquid Phase Conjugates:

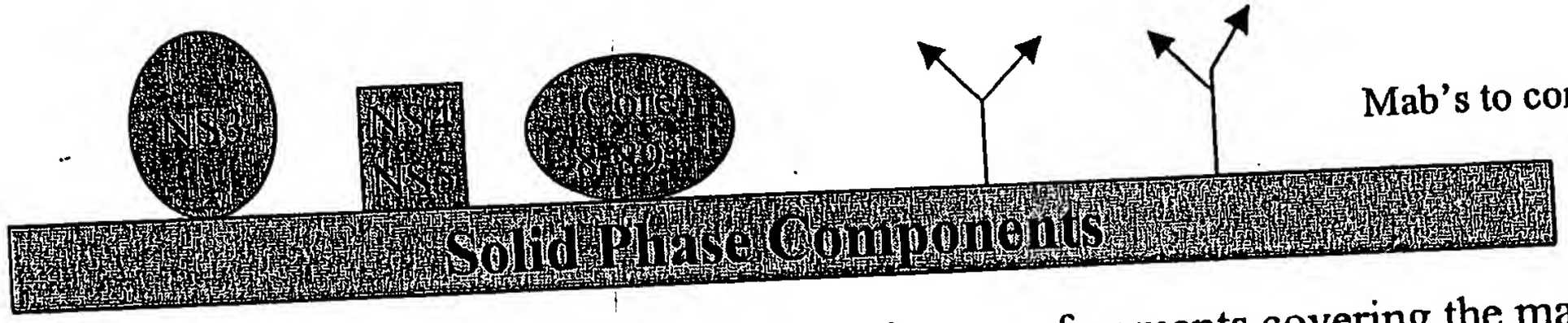
Goat anti-human conjugate
- detect antibodies to core, NS3-5

Conjugated mab's to core
- detects core antigen in serum
- conjugates must not recognize solid phase core

Mab's agst aa:

1-8, 89-190, 8-89

(amino acid deletions substitutions are made in core solid phase proteins/peptides)



Mab's to core 1-8, 89-190

*Recombinant core aa 8-89 may appear as a single entity or as fragments covering the major epitopes…sequences may be modified by deletions, substitutions between aa 8-89 that do not perturb major epitopes. Synthetic peptides covering aa 8-89 would also be a viable alternative.

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